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EXAMINER	
SULLIVAN, DANIEL M	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 09/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/992,957	HERWEIJER ET AL.	
	Examiner	Art Unit	
	Daniel M. Sullivan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 July 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,9-12 and 25-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7, 9-12 and 25-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is a reply to the Paper filed 22 July 2005 in reply to the Non-Final Office Action mailed 16 February 2005. Claims 1-7, 9-12 and 25-27 were considered in the 16 February Office Action. Claims 1, 12 and 25 were amended in the 22 July Paper. Claims 1-7, 9-12 and 25-27 are pending and under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Amendment and Arguments

Claim Rejections - 35 USC § 102

Rejection of claims 25-27 under 35 U.S.C. 102(b) as being anticipated by Böhm *et al.* (1998) *Vaccine* 16:949-954 is **withdrawn**. Amended claim 25 is now limited to providing a non-viral nucleic acid encoding at least one antigenic determinant of said antigen. In the method of Böhm *et al.*, the antigen is the hepatitis B surface antigen, which is encoded by a viral (*i.e.*, hepatitis B virus) nucleic acid.

Claims 1-6 and 9-12 **stand rejected** under 35 U.S.C. 102(b) as being anticipated by either one of Liu *et al.* or Zhang *et al.* for reasons of record and herein below.

Response to Arguments

In response to the *prima facie* case and arguments of record, Applicant has amended claim 1 to recite in part (e), "generating the immune response in a majority of mammals injected for the purpose of utilizing the immune response, such use is selected from the list consisting of..." In the remarks, Applicant contends that the teachings of Liu and Zhang do not apply because the claims now positively recite the use of their method. Applicant urges, "Applicants purposely create the immune response and use it as part of their method".

These arguments have been fully considered but are not deemed persuasive. The amended claims do not recite process steps related to using the immune response generated in the animal. Instead, the claims merely recite that the process steps recited are performed "for the purpose of utilizing the immune response". To avoid the prior art a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 370 F.2d 576, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 312 F.2d 937, 939, 136 USPQ 458, 459 (CCPA 1963). As established in the previous Office Actions, there is no manipulative difference between the process claimed in the instant application and the process disclosed in the prior art.

As described in the Office Action mailed 7 September 2004 (page 7-9), both Liu *et al.* and Zhang *et al.* teach a method comprising providing a plasmid DNA encoding an antigenic peptide (*i.e.*, luciferase; demonstrated in Example 5, page 41-42, of the instant application to be

antigenic); injecting the nucleic acid into a vessel connected to a tissue of a mammal (*i.e.*, a mouse tail vein); and elevating intravascular pressure and increasing permeability, thereby delivering said nucleic acid sequence to an extravascular cell in said tissue and obtaining expression of luciferase in various organs and tissues of mice, which is demonstrated in Example 5 of the instant application to elicit an immune response. Furthermore, Example 8 of the instant application demonstrates that this process, practiced in mice, results in an antibody response in a majority of the mice injected.

As the process steps recited in the instant claims are the same as the process steps taught by Liu *et al.* and Zhang *et al.* and there is nothing of record that would indicate that the intended use recited in the instant claims results in a manipulative difference between what is presently claimed and the method of Liu *et al.* and Zhang *et al.*, merely reciting that the process is practiced for the purpose of utilizing an immune response does not distinguish the claims from the art.

Applicant's arguments have been fully considered but are not deemed persuasive in view of the record as a whole. Therefore, the claims stand rejected under 35 USC §102(b) as anticipated by the art.

Claims 25-27 **stand rejected** under 35 U.S.C. 102(b) as being anticipated by Hurpin *et al.* (1998) *Vaccine* 16:208-215 (made of record in the IDS filed 12 January 2005).

As stated in the previous Office Action, Hurpin *et al.* teaches a method of generating antibodies specific to an antigen (*i.e.*, p53) comprising providing a nucleic acid encoding said antigen (*i.e.*, a canary pox vector (ALVAC) comprising the nucleic acid) and injecting the

nucleic acid into the tail vein of a rodent (see especially the first full paragraph in the right column on page 209 and the first full paragraph in the right column on page 210). Hurpin *et al.* further teaches that the ALVAC vector provides expression in the liver (see especially the second full paragraph on page 210 and Table 1) and assays for anti-p53 antibodies in the immunized mice, which would include the step of isolating said antibodies from said mouse. Therefore, the method of Hurpin *et al.* comprises each of the process steps of the instant claim 25 and is practiced with a mouse according to claim 27. Furthermore, the canary pox vector comprises the vector nucleic acid complexed with viral proteins, which viral proteins are polymers according to the limitations of claim 26.

Response to Arguments

In response to the *prima facie* case of record, Applicant has amended claim 25 to recite providing "a non-viral nucleic acid encoding at least one antigenic determinant of said antigen" and contends that the teachings of Hurpin *et al.* do not apply to the claims because, "Hurpin *et al.* observed an immune response after injection of viral vector into the tail vein of mice" (page 5 of the Remarks).

This argument has been fully considered but is not deemed persuasive because it is based on an overly narrow reading of the claims. According to the broadest reasonable interpretation of the phrase, "a non-viral nucleic acid encoding at least one antigenic determinant of said antigen" requires only that the nucleic acid encoding the at least one antigenic determinant be a non-viral nucleic acid. Although the nucleic acid of Hurpin *et al.* is delivered using a viral vector, the nucleic acid itself is a human p53 encoding nucleic acid (see especially the second full paragraph

on page 209). Therefore, the method of Hurpin *et al.* comprising providing a human p53 in an ALVAC vector reads on the claimed invention according to the broadest reasonable interpretation thereof.

Applicant's arguments have been fully considered but are not deemed persuasive in view of the record as a whole. Therefore, the claims stand rejected under 35 USC §102(b) as anticipated by the art.

Claim Rejections - 35 USC § 103

Claim 7 **stands rejected** under 35 U.S.C. 103(a) as being unpatentable over Liu *et al.* or Zhang *et al.* and further in view of Smyth-Templeton *et al.* for reasons of record and herein below.

As above, in response to the *prima facie* case and arguments of record, Applicant contends that the teachings of Liu and Zhang do not apply to the amended claims because the claims now positively recite the use of their method. These arguments have been fully considered but are not deemed persuasive because the intended use recited in the instant claims does not result in a manipulative difference between what is presently claimed and the method of Liu *et al.* and Zhang *et al.* Therefore, merely reciting that the process is practiced for the purpose of utilizing an immune response does not distinguish the claims from the art.

Applicant's arguments have been fully considered but are not deemed persuasive in view of the record as a whole. Therefore, the claims stand rejected under 35 USC §103(a) as obvious over the art.

New Grounds Necessitated by Amendment

Claim Objections

Claim 1 is objected to because of the following informalities: In the third line of part (d), the word "cell" has been omitted from the phrase "nucleic acid in said cell". This appears to have been an inadvertent error and the claim has been examined with the assumption that the limitation "said cell" is still present. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7, 8-12 and 25-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims have been amended to recite generating the immune response "in a majority of mammals" (independent claim 1) or expressing antigen "in a majority of the injected rodents" (independent claim 25). It is unclear from the disclosure whether these phrases require that the immune response or expression be generated in a majority of mammalian or rodent species or strains of mice, or whether the limitation requires that the majority of subjects within a treated population of a single species or strain exhibit an immune response or antigen expression. For example, it is unclear whether a process that provides an immune response in 100% of individuals within a single species of mammal but does not elicit an immune response in any other species of mammal would read on claim 1. Conversely, it is unclear whether a process that

provides an immune response in a minority of individuals within any given mammalian species but elicits an immune response in 100% of mammalian species would read on the claim. As the scope of the claims is subject to alternative interpretations and it is unclear from the disclosure which interpretation defines the subject matter claimed, the metes and bounds of the claims is unclear.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7, 9-12 and 25-27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The MPEP states, "[i]f new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. §112, first paragraph-written description requirement. *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." (MPEP § 2163.06). The MPEP further states, "[w]henever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not

described in the application" (*Id.*, § 2163.02). The introduction of claim changes which involve narrowing the claims by introducing elements or limitations which are not supported by the as-filed disclosure is a violation of the written description requirement of 35 U.S.C. 112, first paragraph. See, e.g., Fujikawa v. Wattanasin, 93 F.3d 1559, 1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996).

In the instant case, the claims have been amended to recite generating the immune response "in a majority of mammals" (independent claim 1) or expressing antigen "in a majority of the injected rodents" (independent claim 25). Applicant's submission does not include any statement as to where support for these limitations can be found in the originally filed disclosure and the Examiner can find no literal support for a process limited to generating an immune response in a majority of mammals injected or expressing antigen in a majority of injected rodents. The closest teaching is found in Example 8, wherein eight mice were immunized with a plasmid encoding a luciferase transgene and an antibody response was detected in a majority of the mice injected (see also Figures 3 and 4). However, there is nothing in this teaching that would lead the skilled artisan to the more generic limitations now recited in the claims because the specification does not disclose obtaining an immune response or antigen expression in a majority of injected mammals or rodents as a general property of the disclosed method. In the absence of such generic teaching, the skilled artisan would not have viewed the specific example of an antibody response elicited in a majority of mice injected with a plasmid comprising a luciferase transgene as clearly conveying the limitation of a process to obtaining any immune response other than an antibody response in a majority of mammals (regardless of how the limitation is construed, *Id.*) or to obtaining an antibody response in a majority of any species of

mammal other than a mouse injected with a construct comprising a luciferase transgene. Likewise, the skilled artisan would not have viewed the example as supporting claims limited to a process wherein a nucleic acid is delivered to a liver cell, wherein antigen is expressed in a majority of injected rodents. Therefore, the limitation of the claims to generating an immune response "in a majority of mammals" or expressing antigen "in a majority of the injected rodents" constitutes impermissible new matter.

Claim 25 has also been amended such that the injected nucleic acid encoding at least one antigenic determinant of an antigen is limited to "a non-viral nucleic acid". Again, Applicant's remarks do not include a statement as to where the newly added limitation can be found in the originally filed disclosure. As discussed above, the limitation is construed as requiring that the nucleic acid encoding the antigenic determinant be a non-viral nucleic acid. The Examiner can find no literal support for the claimed process limited to delivering a non-viral nucleic acid encoding an antigenic determinant. The closest teachings are found in the section entitled "*In Vivo* Transfection Reagents" commencing on page 12 of the specification, which discusses delivery of nucleic acids using "non-viral particles". However, nothing in this section would lead the skilled artisan to limitation of the disclosed method to injection of a non-viral nucleic acid encoding at least one antigenic determinant of an antigen as newly recited in the claim. Therefore, the limitation constitutes new matter added to the disclosure.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP §.706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M. Sullivan whose telephone number is 571-272-0779. The examiner can normally be reached on Monday through Thursday 6:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Daniel M. Sullivan, Ph.D.
Examiner
Art Unit 1636

DANIEL M. SULLIVAN
PATENT EXAMINER